Comments of the American Clinical Laboratory Association on Stimulating Innovation in Medical Technologies

[Docket No. 2004S-0233]

The American Clinical Laboratory Association ("ACLA") is pleased to submit these comments on the Department of Health and Human Services' ("HHS") efforts to stimulate innovation in medical technologies. *See* 69 Fed. Reg. 61018 (Oct. 14, 2004). ACLA is an association representing independent clinical laboratories throughout the United States including local, regional and national laboratories. In the United States alone, clinical laboratories perform millions of tests each year for physicians and other health care professionals. ACLA members are regularly engaged in the development and performance of new types of testing to help physicians diagnose, treat, and/or monitor various medical conditions. As a result, ACLA members are very interested in HHS's initiative to stimulate innovation in medical technology.

Clinical laboratory testing is an important, cost-effective and life saving health care tool, which provides physicians with objective medical information about a patient's condition. Appropriate testing ultimately enhances health, saves lives and reduces health care costs. Independent clinical laboratories are an important participant in that process. Laboratories play an integral role in the development of new health care technology. Many of the newest tests currently being made available to practitioners and patients are developed in the laboratory, using analyte specific reagents ("ASRs") and tests that incorporate multiplex technology. These technological advances allow the laboratory to analyze a multitude of factors that help practitioners more specifically identify and diagnose patient conditions and provide more focused and effective treatment for those conditions. Accordingly, so as not to chill the adoption of innovative technology, ACLA believes that it is vitally important for applicable regulatory schemes to keep up with the advances in clinical laboratory technology. Regulatory bodies must take into account and respond quickly to changes in technology to avoid being an obstacle to the development of these innovative products and services that improve patient care.

ACLA believes there are a number of different barriers to making new, high quality, life-saving technologies available to patients in an efficient and effective manner, and we appreciate the opportunity to share our thoughts with the agency on these issues. In particular, we believe some of the obstacles to innovation include:

- agency efforts to unnecessarily impose more burdensome regulatory schemes, specifically in areas relating to analyte specific reagents ("ASRs") and multiplex testing;
- the agencies' inability to respond efficiently and consistently to rapid changes in health care technology, including with respect to establishing clear and consistent regulatory pathways for assessment of new technology; and

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- the need for funding and a more substantial governmental role in developing data on the clinical value of new technology, as well as better and more efficient regulatory processes for coverage and reimbursement decisions.

Agency Efforts to Impose More Burdensome Regulatory Schemes

The regulatory system for determining how a device is regulated by the FDA is outdated and illogical. Determining coverage for technologies developed in the 21st century based on whether there was a similar product in commercial distribution in 1976 is not appropriate or reasonable. Furthermore, the regulatory procedures in the United States focus too much on pre-market requirements instead of post-market surveillance, which gives a more realistic assessment of how products actually meet clinical standards. Accordingly, we recommend that HHS consider exploring legislative and regulatory changes to lessen the focus on premarket review and to take into account more fully what occurs once the medical technology is on the market.

FDA regulation, and the threat of regulation, is already slowing the adoption of new technology in a number of areas, including genetic testing and pattern expressions. Furthermore, ACLA is concerned that the lack of clarity on the appropriate level of regulation for certain in vitro diagnostic tests is stifling the innovation that could be achieved in this field. In particular, agency statements regarding analyte specific reagents and multiplex testing seem to serve only to impede the development and marketing of new health care technology.

Analyte Specific Reagents

In recent years, the FDA has increasingly stated that it is considering further regulation of the clinical laboratory industry, despite the comprehensive regulatory framework already in place as a result of the Clinical Laboratory Improvement Amendments ("CLIA").[1] Under CLIA, all labs must be federally certified, and must meet federal quality assurance, proficiency testing, and personnel standards. All laboratory developed tests must meet certain quality control standards. Recently, the FDA has attempted to regulate certain testing developed by labs, even though these tests are also regulated under CLIA. For instance, besides the Draft Guidance on multiplex testing (discussed more fully below), the FDA has also issued Draft Guidance regarding premarket notifications for in vitro HIV drug resistance genotype assays.[2] Furthermore, under the auspices of the Secretary's Advisory Committee on Genetic Testing, the FDA has also considered additional oversight of genetic tests.[3]

Laboratories are already subject to extensive oversight and regulation under CLIA. In all of the instances mentioned above, the proposed regulatory actions would overlap with and duplicate the existing regulations that govern clinical laboratory practice. It would be more logical and reasonable to require any additional oversight of the clinical laboratory industry to be accomplished within the existing CLIA framework instead of creating entirely new, burdensome, and overlapping regulatory requirements.

[1] *See* 42 C.F.R. §493.1 *et seq*.
[2] *See* 66 Fed. Reg. 45683.
[3] *See* 65 Fed Reg. 77631.

We are especially concerned about recent indications from FDA officials that they are reconsidering the current regulatory scheme for laboratory testing that involves the use of "analyte specific reagents" ("ASRs"), which are the active components in many laboratory-developed tests, especially genetic tests. In the ASR regulation, issued in November 1997, the FDA stated that most ASRs would be considered Class I and therefore exempt from pre-market approval or clearance by the FDA.[4]

FDA officials have repeatedly stated that they are considering a revision of the ASR rule. While we have seen no draft proposals, statements from the FDA indicate they are considering a revision of the ASR rule that might require higher standards for approval or clearance of the ASRs or might even require laboratories to obtain FDA approval or clearance for certain "high risk"[5] laboratory-developed tests. While much of the discussion has focused on genetic testing, FDA officials have indicated that their concerns are not limited to genetic testing.

The current regulation of ASRs is appropriate and serves the twin goals of fostering innovation and ensuring patient safety. However, recurrent efforts by the agency to add new regulatory burdens creates uncertainty in the marketplace, which has a negative effect on innovation by discouraging parties from investing in such technologies and products. We recommend that the FDA not take any specific actions to further regulate ASRs or genetic testing. The CLIA program appropriately oversees the development and use of these tests, and it is possible that the CLIA regulations will be specifically amended to address genetic testing in more detail in the near future.

Multiplex Testing

In addition, FDA's efforts to further regulate tests using multiplex technology are troubling. These types of tests are the future of the laboratory industry, and FDA appears to be taking an overly formalistic approach to consideration of these technologies. On April 21, 2003, the Center for Devices and Radiological Health issued draft guidance for industry ("Draft Guidance") regarding multiplex tests for heritable DNA markers, mutations and expression patterns. Specifically, ACLA is concerned that the agency is seeking to improperly use the Draft Guidance to narrow the scope of the ASR regulations or disrupt the flow of reagents that incorporate multiplex technology. Multiplexed assays have many advantages over equivalent panels of separately-performed assays (*e.g.*, automation, the need for only a small sample volume, and enhanced quality assurance), but in all other respects, are technically the same as running the component tests sequentially or in parallel. Yet, the FDA argues that running multiple tests at once on standard automated equipment requires its oversight, while running the same tests in sequence does not.

On its face, the Draft Guidance addresses only the data requirements for premarket approval ("PMA") and 510(k) submissions for devices that incorporate multiplex technology. The Draft Guidance does not purport to define the boundary between clinical assays which

[4] *See* 62 Fed. Reg. 62243 (Nov. 21, 1997). The ASR rule did indicate that some tests for contagious diseases, such as tuberculosis or HIV, would be considered Class III, and thus subject to FDA pre-market clearance or approval. *See* 21 C.F.R. § 864.4020(b).

[5] At this point, "high risk" has not been defined.

incorporate multiple ASRs (which are exempt from pre-market approval in accordance with the ASR Rule[6]), and devices that incorporate multiplex technology and are complete "test systems" and therefore require FDA approval. Because the Draft Guidance did not address the question of this boundary, ACLA is concerned that many ASRs used in laboratory-developed tests today might arguably be construed to come within the scope of this Draft Guidance.

In our comments to FDA, we requested that the Draft Guidance be clarified to state that it is not intended to revise the ASR rule and does not mandate FDA approval of multiplex reagents where each of the multiplex reagents otherwise meets the definition of a Class I ASR. We continue to make this recommendation to the agency. If the FDA goes forward with the Draft Guidance in its current form, manufacturers may choose to simply sell the individual analytes to clinical laboratories and provide the laboratories with the instructions for how they should be mixed to perform the particular testing service. However, we do not believe this would benefit patient care. It is our understanding that FDA will be finalizing its guidance on these issues by the end of the year, and we want to reiterate our opposition to any categorization that creates additional burdens for testing that incorporates multiple reagents instead of a single reagent. We do not believe such a distinction serves any purpose, as long as each reagent otherwise meets the definition of a Class I ASR. Thus, we highlight this as an example of the obstacles to encouraging innovation in medical technology. Such action only serves to impede new developments in this area, and evidences a limited view of the value of these types of technological advances.

In addition, in 2003, the Office of In Vitro Diagnostic Devices ("OIVD") reviewed the microarray marketed by Roche Molecular Diagnostics under the trade name AmpliChip™, and set out another standard for analysis of multiplex testing. While Roche advocated that the AmpliChip fit within the definition of a Class I ASR, OIVD ultimately determined that it was unnecessary to reach a conclusion on this question because even if it were to qualify as an ASR, the product would lose its Class I, 510(k)-exempt status because its intended use (to identify polymorphisms related to drug metabolism) was "of substantial importance in preventing impairment of human health."[7] OIVD further stated that the technological characteristics of the AmpliChip would "cause it to differ from existing or reasonably foreseeable ASRs such that the AmpliChip would not be exempt from premarket notification." Thus, OIVD used another standard to evaluate this technology, which is not entirely clear or consistent with previous agency guidance, thereby creating additional confusion for providers and companies attempting to comply with the regulatory requirements applicable to new health care technologies. However, the laboratory industry considers such multi-array chips to be merely another form of multiplex technology in which multiple, simultaneous ASRs are used to perform a test at one time rather than sequentially.

In sum, we are concerned that the FDA is improperly seeking to regulate by making public statements about its authority to regulate genetic tests, by its use of Draft Guidance that is often never finalized, and by enforcement examples based on unclear standards. As a result, there is a consistent lack of predictability in the industry, which disrupts the innovation in

[6] *See* 62 Fed. Reg. 62243.
[7] *See* Letter from OIVD to Heinrich Dreismann, dated October 29, 2003.

technology that providers are working to achieve because there is no clear articulation of the regulatory standards.

Inability to Respond to Rapid Changes in Health Care Technology

ACLA would like to work with the FDA and the Centers for Medicare and Medicaid Services ("CMS") to ensure that these agencies are efficiently and consistently able to respond to rapid changes in health care technology, including with respect to establishing payment for new technology and certain FDA approval requirements. Given the importance of advancing patient care and the pace of innovation in these areas, we believe it is critically important for the agencies to be nimble in their consideration of new technologies, willing to resolve coding and payment issues at an early date, and open to interactions with stakeholders.

Establishing Payment for New Technology

CMS' responsibility to establish and follow fair procedures for coding and payment determinations is of great importance to the laboratory industry because Medicare is the largest single third-party payor in the U.S., covering approximately 40 million beneficiaries. In addition, the local carriers' Medicare fee schedules, limited by the National Limitation Amount ("NLA"), automatically set the upper limit on Medicaid's payment for clinical laboratory tests. Further, many commercial payors set their clinical laboratory fees based on Medicare payment levels. Thus, Medicare coding and payment determinations significantly impact and essentially drive the payment levels for most clinical laboratory testing in this country. Unfortunately, however, the process for obtaining a CPT code for a new clinical laboratory test is both burdensome and inefficient.

The current clinical laboratory fee schedule was developed in 1984, based on a survey of prevailing rates at the time. It is widely recognized that there were flaws in the data on which the fee schedule was based. Furthermore, that data – which is now 20 years old – does not reflect the incredible changes in industry technology that have occurred over this time period. There are no standards governing how new types of testing should be paid for, nor is there a process that provides accountability for the coding and payment determinations that are made. This lack of predictability ultimately inhibits innovation and the development of new testing processes.

For new tests that are not already covered by the laboratory fee schedule, CMS has developed an "ad hoc" methodology to determine pricing. For some tests, CMS directs carriers to develop their own prices, based on "gap filling." Presumably, carriers are to determine the price that is applicable in their individual area, but CMS has provided little guidance to carriers concerning what information they are to review to develop the new gap filled prices. Once all the carriers have set prices by gap filling, CMS then establishes the NLA for those tests at 100 percent of the median of the carriers' fee schedule prices for those tests.

In other instances, CMS simply "cross-walks" a new CPT code to an existing code, and prices the new code at the same level as the old code. However, there may be little technological relationship between the new test and the old one; therefore, the decision to price them at the same level often results in inappropriate payments. In recent years, CMS has almost exclusively used the cross-walking method, which means that providers are not receiving fair payment for

more costly, but more accurate new technology. Moreover, when new codes are cross-walked to existing ones, the NLA remains the same, which is completely inconsistent with the process used for gap filling. Since new tests are usually linked to the prices being paid for old tests, this coding and payment system only serves to compound the financial problems already experienced by clinical laboratory providers because their fee schedule is based on outdated data.

The Medicare, Medicaid and SCHIP Benefits Improvement and Protection Act of 2000 ("BIPA") mandated that CMS establish new procedures for coding and payment determinations for new clinical laboratory tests, including an opportunity for public consultation. Pursuant to BIPA, last year CMS established a new process for receiving public input on the proposed codes for the Medicare Clinical Laboratory Fee Schedule. In addition, the Medicare Modernization Act ("MMA") included provisions further revising this process, but these provisions have not yet been implemented. However, these procedures do not go anywhere near far enough because CMS has failed to establish any standards that apply to the cross-walk and gap fill processes.

One major problem with the current system is that existing abnormally low carrier fees continue to disadvantage labs when CMS cross-walks to inappropriate codes. Because there are no published, fair and binding criteria for CMS' cross-walk determinations, this approach has led to arbitrary coding determinations in the past. This approach allows CMS to map a new test to an older code for the same type of test, even if the new test uses a vastly different (and more costly) technology.

In addition, carriers do not receive clear instructions on the criteria to use to gap fill a local payment rate. In recent years, CMS has used the more objective gap fill process less and less frequently. For instance, the gap fill method accounted for only 2% of new tests in 2001, compared to 76% of all new tests in 1994. According to Raab and Logue, the cross-walk approach allows CMS to "use its discretion in mapping new codes to codes already on the fee schedule, whose payment rates are compatible with CMS' preferences for what the payment should be for the new test."[8] Moreover, the lack of established standards for gap filling also leads to unreasonable variation among carriers in the fee levels that they ultimately set.

In order to promote the delivery of high quality, timely, and efficient health care, CMS must pay fairly for new types of technology. Specifically, we urge CMS to:

- Establish an open, timely and acceptable process that is subject to the rights of affected parties to due process and appeal, and which does not impede clinical decision-making that is essential to providing appropriate care.

- Efficiently implement the Medicare Modernization Act provisions that require CMS to issue a proposal for how it intends to pay for new tests; provide an opportunity for affected parties to meaningfully comment on such proposals; and respond to comments. In addition, this process should permit stakeholders an opportunity to appeal adverse determinations.

[8] G. Gregory Raab and L. Joan Logue, *Medicare Coverage of New Clinical Diagnostic Laboratory Tests: The Need for Coding and Payment Reforms*, Clinical Leadership & Management Review, November/December 2001, at 376, 380.

- Develop clear standards concerning how carriers determine payment levels in their jurisdictions, and require carriers to examine, adjust and/or justify significant existing local carrier payment variations from the NLAs.

- Establish criteria for determining whether a new CPT code will be cross-walked to an existing code or gap filled.

- When it is determined that a new CPT code will be cross-walked, CMS should specify the factors that will be considered in identifying the appropriate code to which the new test is cross-walked.

- For tests that will be gap filled, CMS should establish clear standards for the types of information that carriers will consider in establishing a gap filled price.

- Ease restrictions on the units of service for laboratory testing, which are often arbitrary and impede the development and use of cutting-edge technology.

- Consider implementing adjustments to the HCPCS temporary coding process to allow the issuance of temporary codes in a more timely fashion so that providers can bring new testing services to patients more quickly.

Certain FDA Approval Requirements

There is considerable overlap between the FDA's requirements for approval of new devices and the CMS requirements for coverage of new products and services. In many cases, this leads to incredible difficulties for the providers and manufacturers that must navigate and coordinate these processes in order to bring a new technology to Medicare beneficiaries. Agency policies that prevent communication between the FDA and CMS contribute to and exacerbate these difficulties. For instance, the FDA is mandated to adhere to very strict confidentiality policies, which prevent the agency from sharing information even with CMS so that CMS can make important Medicare coverage decisions. However, CMS only observes the restrictions imposed by the Freedom of Information Act. Disparate policies like these create additional hurdles for providers attempting to secure the necessary clearances for new health care technology. Accordingly, ACLA recommends that HHS streamline these types of policies to allow its agencies to better coordinate with each other, including concurrent review of new technologies by FDA and CMS with the applicant's consent, to make innovative products and services available more quickly to beneficiaries that may benefit from them.

Need for Funding and More Supportive Government Role in Developing Data, as well as More Efficient Regulatory Processes for Coverage and Reimbursement Decisions

Another significant obstacle to innovation is the need for funding and a more substantial governmental role in developing data on the clinical value of new technology. The government should partner with industry to explore ways to develop better data on the clinical utility of certain new medical technologies. One way to support this effort would be to designate some federal funding for public/private partnerships to research and create these processes. The government must play a more supportive role in determining when technology merits coverage

and reimbursement, including providing funding for large-scale studies to determine clinical utility.

In order to promote the development of new medical technologies, HHS must also establish better and more efficient regulatory processes for reimbursement decisions. Developers of new technology often do not have a clear and unambiguous regulatory pathway (which would allow them to estimate costs of development) or any indication whether the technology will be covered by Medicare or other payers. In addition to addressing the reimbursement system, HHS should create a simple initial review process that involves all its constituencies to help technology developers better estimate the costs (regulatory compliance) and the potential revenues of their technologies. FDA could consider using panels of outside experts to review new technology and recommend the appropriate regulatory pathway and requirements (which, if followed, would lead to clearance or approval).

Under the current system, every insurer, as well as the Medicare program, has a separate and distinct process for evaluating the coverage and reimbursement for new health care technology. These disparate assessment systems create an unreasonable burden on those providers seeking approval of new medical technologies. Furthermore, they slow the development processes tremendously, making it even more difficult to deliver new, life-saving technologies to patients. Earlier review, by a recognized body, would make the technology assessment process easier and more efficient. Ultimately, such regulatory clarity would save money for the health care system and speed the delivery of innovative new health care treatments to patients and practitioners. These types of assessment bodies should meet more frequently and that providers should be able to receive advice more quickly on coverage issues.

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Thank you for the opportunity to submit these comments. We are looking forward to working with HHS to develop and implement effective strategies for encouraging innovation in medical technology.